Temporal Trends and Outcomes of Left Ventricular Aneurysm After Acute Myocardial Infarction



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There are limited data on the prevalence and an outcome of left ventricular (LV) aneurysms following acute myocardial infarction (AMI). Using the National Inpatient Sample during 2000 to 2017, a retrospective cohort of AMI admissions was evaluated for LV aneurysms. Complications included ventricular arrhythmias, mechanical, cardiac arrest, pump failure, LV thrombus, and stroke. Outcomes of interest included in-hospital mortality, temporal trends, complications, hospitalization costs, and length of stay. A total 11,622,528 AMI admissions, with 17,626 (0.2%) having LV aneurysms were included. The LV aneurysm cohort was more often female, with higher comorbidity, and admitted to large urban hospitals (all p < 0.001). In 2017, compared with 2000, there was a slight increase in LV aneurysms prevalence in those with (adjusted odds ratio [aOR] 1.57 [95% confidence interval {CI} 1.41 to 1.76]) and without (aOR 1.13 [95% CI 1.00 to .127]) STsegment-elevation AMI (p < 0.001 for trend). LV aneurysms were more commonly noted with anterior ST-segment-elevation AMI (31%) compared with inferior (12.3%) and other (7.9%). Ventricular arrhythmias (17.6% vs 8.0%), mechanical complications (2.6% vs (0.2%), cardiac arrest (7.1% vs 5.0%), pump failure (26.3% vs 16.1%), cardiogenic shock (10.0% vs 4.8%) were more common in the LV aneurysm cohort (all p < 0.001). Those with LV aneurysms had comparable in-hospital mortality compared with those without (7.4% vs 6.2%; aOR 1.02 [95% CI 0.90 to 1.14]; p = 0.43). The LV aneurysm cohort had longer length of hospital stay, higher hospitalization costs, and fewer discharges to home. In conclusion, LV aneurysms were associated with higher morbidity, more frequent complications, and greater in-hospital resource utilization, without any differences in in-hospital mortality in AMI. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;133:32-38)

A left ventricular (LV) aneurysm is an uncommon complication following acute myocardial infarction (AMI) that is thought to complicate about 1/3 of all Q-wave AMIs.¹ Data from studies performed about 2 decades ago demonstrated decrease in the incidence of LV aneurysms, primarily due to the introduction of thrombolytic therapy.² In the current era, this complication is seen less frequently and is confirmed by mainly case reports and sparse case series. The European and American Heart Association/American College of Cardiology guidelines on ST-segment elevation estimate the incidence of LV aneurysms as <5%.^{3,4} Parallel to these advancements in the treatment, improvement in imaging techniques and surgical approaches to aneurysm repair have been noted.⁵ The improvement in care models of patients with acute coronary syndrome with better management of heart failure, shorter door-to-balloon time in patients with STEMI, increase in the proportion of patients with non-ST-segment elevation myocardial infarction (NSTEMI) and growing number of elderly patients with AMI are likely to have affected the incidence of LV aneurysm in the contemporary era. We accordingly used a large national database to assess the prevalence and outcomes of LV aneurysm in AMI.

Methods

The National (Nationwide) Inpatient Sample (NIS) is the largest all-payer database of hospital inpatient stays in the United States. NIS contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Quality and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.⁶ Information regarding each discharge includes patient

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demographics, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses, and procedural diagnoses. The HCUP-NIS does not capture individual patients but captures all information for a given admission. Institutional Review Board approval was not sought due to the publicly available nature of this deidentified database. These data are available to other authors via the HCUP-NIS database with the Agency for Healthcare Research and Quality. This research was done without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes or interpret the results. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

Using the HCUP-NIS data from 2000 to 2017, a retrospective cohort study of adult admissions (>18 years) with AMI in the primary diagnosis field (International Classification of Diseases 9.0 Clinical Modification [ICD-9CM] 410. x and ICD-10CM I21.x-22.x) were identified. Similar to previous literature, we identified LV aneurysm using ICD-9CM 414.10 and ICD-10CM I25.3.^{7,8} We excluded admissions that did not have information on in-hospital mortality. The Deyo's modification of the Charlson Comorbidity Index was used to identify the burden of co-morbid diseases (Supplementary Table 1). $^{9-11}$ Demographic characteristics, hospital characteristics, use of coronary angiography, percutaneous coronary intervention (PCI), thrombolysis, mechanical circulatory support, acute noncardiac organ failure, and noncardiac organ support use were identified for all admissions using previously used methodologies from our group.¹²⁻¹⁸ Similar to previous literature, we identified timing of coronary angiography and PCI relative to the day of admission, and defined early coronary angiog-raphy as that performed on hospital day zero.^{15,19–22} Complications were classified as (1) ventricular arrhythmias ventricular tachycardia or fibrillation; (2) mechanical ventricular septal defect, papillary muscle rupture, hemopericardium and cardiac tamponade; (3) cardiac arrest; (4) pump failure - cardiogenic shock, systolic heart failure and acute respiratory failure; (5) LV thrombus formation, and (6) ischemic or hemorrhagic stroke.

The primary outcome was the in-hospital mortality in AMI admissions with and without an LV aneurysm. The secondary outcomes included temporal trends of LV aneurysm and in-hospital mortality, rates of complications, hospital length of stay, hospitalization costs and discharge disposition in AMI admissions with and without an LV aneurysm. Multiple subgroup analyses classified by age (\leq />75 years), sex, race (white/non-white), type of AMI (STEMI vs NSTEMI), and receipt of PCI were performed to identify high-risk cohorts.

As recommended by HCUP-NIS, survey procedures using discharge weights provided with HCUP-NIS database were used to generate national estimates.²³ Using the trend weights provided by the HCUP-NIS, samples from 2000 to 2011 were reweighted to adjust for the 2012 HCUP-NIS redesign.²³ Chi-square and *t* tests were used to compare categorical and continuous variables, respectively. Multivariable logistic regression was used to analyze trends over time (referent year 2000). Univariable analysis for trends and outcomes was performed and was represented as odds

ratio (OR) with 95% confidence interval (CI). Multivariable logistic regression analysis incorporating age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, hospital bedsize, type of AMI, cardiogenic shock, cardiac arrest, acute kidney injury, ventricular tachycardia/fibrillation, mechanical complications, pump failure, stroke, left ventricular thrombus, fibrinolysis, coronary angiography, PCI, coronary artery bypass grafting, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis was performed for assessing in-hospital mortality. For the multivariable modeling, regression analysis with purposeful selection of statistically (liberal threshold of p < 0.20 in univariate analysis) and clinically relevant variables was conducted.

The inherent restrictions of the HCUP-NIS database related to research design, data interpretation, and data analysis were reviewed and addressed.²³ Pertinent considerations include not assessing individual hospital-level volumes (due to changes to sampling design detailed above), treating each entry as an "admission" as opposed to individual patients, restricting the study details to inpatient factors since the HCUP-NIS does not include outpatient data, and limiting administrative codes to those previously validated and used for similar studies. Two-tailed p < 0.05 was considered statistical comparisons will be significant, however need careful interpretation for clinical significance. All statistical analyses were performed using SPSS v25.0 (IBM Corp, Armonk, New York).

Results

In the period from January 1, 2000 to December 31, 2017, there were 11,622,528 admissions for AMI, of which LV aneurysm was noted in 17,626 (0.2%). Compared with those without LV aneurysms, those with LV aneurysms had higher comorbidity and were admitted to large urban hospitals (all p < 0.001) (Table 1). LV aneurysms were noted to complicate 0.2% to 0.3% of all STEMI and 0.1% to 0.2% of all NSTEMI admissions during this 18-year period (Figure 1). Though the overall population had higher rates of NSTEMI, LV aneurysms had comparable STEMI (51%) and NSTEMI admissions, LV aneurysm were more commonly noted with anterior wall involvement (31%) (Table 2).

The cohort with LV aneurysms had higher rates of inhospital complications. Ventricular arrhythmias (17.6% vs 8.0%), mechanical complications (2.6% vs 0.2%), cardiac arrest (7.1% vs 5.0%), pump failure (26.3% vs 16.1%), cardiogenic shock (10.0% vs 4.8%), LV thrombus, and strokes were more common in the LV aneurysm cohort compared to those without (Table 2). The cohort with LV aneurysms had higher unadjusted all-cause in-hospital mortality (7.4% vs 6.2%; OR 1.22 [95% CI 1.15 to 1.29]; p < 0.001), but comparable adjusted in-hospital mortality in a multivariable logistic regression analysis (OR 1.02 [95% CI 0.90 to 1.14]; p = 0.43) (Table 3 and Supplementary Table 2). There was a steady decrease in unadjusted and adjusted in-hospital mortality during the study period across both cohorts

Table 1 Baseline characteristics of AMI admissions with and without LV aneurysm

Characteristic		LV Aneurysm		р
		Yes (N = 17,626)	No (N = 11,604,903)	
Age (years)		68.4 ± 12.9	67.6 ± 14.2	< 0.001
Women		43.2%	39.7%	< 0.001
White race		63.9%	63.6%	< 0.001
Black race		6.7%	7.9%	< 0.001
Other races*		29.5%	28.5%	< 0.001
Primary payer	Medicare	60.9%	57.6%	< 0.001
	Medicaid	6.6%	6.1%	< 0.001
	Private	24.8%	27.9%	< 0.001
	Others [†]	7.7%	8.4%	< 0.001
Quartile of median household income for zip code	0-25th	23.0%	24.4%	< 0.001
-	26th-50th	26.2%	27.2%	< 0.001
	51st-75th	25.0%	24.5%	< 0.001
	75th-100th	25.8%	23.9%	< 0.001
Charlson Comorbidity Index	0-3	30.7%	37.6%	< 0.001
	4-6	52.2%	44.5%	< 0.001
	≥7	17.1%	17.9%	< 0.001
Hospital teaching status and location	Rural	6.3%	11.2%	< 0.001
	Urban nonteaching	35.1%	39.5%	< 0.001
	Urban teaching	58.6%	49.3%	< 0.001
Hospital bed-size	Small	8.7%	11.2%	< 0.001
	Medium	21.8%	25.5%	< 0.001
	Large	69.5%	63.3%	< 0.001
Hospital region	Northeast	19.3%	19.6%	< 0.001
	Midwest	26.8%	22.9%	< 0.001
	South	35.8%	40.1%	< 0.001
	West	18.2%	17.4%	< 0.001
Weekend admission		25.3%	25.8%	0.17

Represented as percentage or mean \pm standard deviation. AMI = acute myocardial infarction; LV = left ventricular.

* Hispanic, Asian or Pacific Islander, Native American, Others.

[†] Self-Pay, No Charge, Others.

(Figure 1). The LV aneurysm cohort had longer length of hospital stay, higher hospitalization costs, and fewer discharges to home and more frequent discharges to skilled nursing facilities (Table 3). To confirm the results of the primary findings and to identify high-risk populations we performed a number of subgroup analyses (Figure 2) which were largely consistent with the primary analyses. In admissions receiving PCI, we noted higher in-hospital mortality in those with LV aneurysms compared with those without.

Discussion

In the largest study evaluating the outcomes of LV aneurysms following AMI, this study noted LV aneurysms to complicated 0.1% to 0.3% of all AMI admissions, with a slightly higher prevalence in STEMI. We noted higher morbidity, more frequent complications, higher incidence of subsequent cardiac and noncardiac procedures and greater in-hospital resource utilization in those with LV aneurysms compared with those without. There were no differences in in-hospital mortality in those with and without LV aneurysms complicating AMI, which was largely consistent in multiple subgroup analyses.

Previous estimates of the incidence of LV aneurysm have varied greatly, largely due to differences in the patient

population, imaging techniques used for its diagnosis, and the advances in medical revascularization management. Data from a stable population of 21,478 consecutive patients enrolled in the Coronary Artery Surgery study from the prereperfusion era, 1,136 (7.6%) patients were identified with LV aneurysm by left ventriculography.²⁴ The diagnosis of aneurysm in that era largely relied on history of AMI, clinical signs and symptoms of congestive heart failure, presence of multivessel coronary artery disease on angiography and detection of aneurysm either by left ventriculography or autopsy. The estimates varied based on the patient population studied from 7.6% as noted in the Coronary Artery Surgery study to 30% to 35% following Q-wave myocardial infarction.^{1,25} In an earlier autopsy study, 3.5% patients developed ventricular aneurysm following healed myocardial infarction.²⁶ Studies from the contemporary era are limited. In an earlier study, only patients who received thrombolytic therapy within 12 hour of symptom onset demonstrated reduction in the incidence of LV aneurysm (7.2 vs 18.8%, p=0.02) underscoring the importance of early and successful reperfusion.² There are no large contemporary studies on the effect of primary PCI on the incidence of LV aneurysm. Mori et al included only patients with anterior AMI; LV apical aneurysm by echocardiogram in a chronic phase developed in

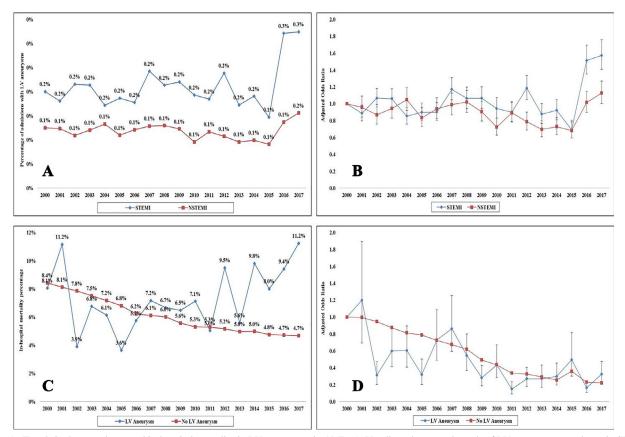


Figure 1. Trends in the prevalence and in-hospital mortality in LV aneurysms in AMI. (*A*) Unadjusted temporal trends of LV aneurysm prevalence in STEMI and NSTEMI (p < 0.001 for trend over time); (*B*) Adjusted odds ratio^a for LV aneurysms prevalence in STEMI and NSTEMI admissions by year (with 2000 as the referent); (p < 0.001 for trend over time); (*C*) Unadjusted in-hospital mortality in AMI admissions with and without LV aneurysm (p < 0.001 for trend over time); (*C*) Unadjusted in-hospital mortality in AMI admissions with and without LV aneurysm (p < 0.001 for trend over time); (*D*) Adjusted odds ratio^b for in-hospital mortality by year (with 2000 as the referent) in AMI admissions with and without LV aneurysm; (p < 0.001 for trend over time). ^aAdjusted for age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, and hospital bed-size. ^bAdjusted for age, sex, race, comorbidity, primary payer, hospital location and teaching status, hospital bedsize, type of AMI, cardiogenic shock, cardiac arrest, acute kidney injury, ventricular tachycardia/fibrillation, mechanical complications, pump failure, stroke, left ventricular thrombus, fibrinolysis, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis. AMI = acute myocardial infarction; LV = left ventricular; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

29 of 161 (18%) patients. Among others, lower final TIMI flow and myocardial blush grade (≤ 2) was associated with the development of LV aneurysm.²⁷

In contrast, our study is the largest to date, contemporary, and reflects the current medical management and revascularization practices across the United States. LV aneurysm was noted in less than 0.4% of all myocardial infarctions and almost equal distribution in STEMI and NSTEMI with higher prevalence noted following anterior infarcts. We noted markedly lower incidence in the primary PCI era as compared with previously noted with thrombolytics or in the prereperfusion eras. This is most likely due to early reperfusion timeline, higher overall success rates for PCI both in the setting of STEMI and NSTEMI, and better heart failure medical management. This could be due to ascertainment bias as routine imaging following AMI is not routinely performed during the index hospital stay and the HCUP-NIS database in an in-hospital database, and cannot follow patients serially in time. LV ejection fraction was missing in 40% of PCIs performed at Mayo Clinic and 19% in rigorously followed cohort study.^{28,29} Lack of consistent cardiac imaging following AMI may lead to inaccurate and lower estimates and we may need rigorous cohort studies for accurate estimation of incidence of LV aneurysm in the current era of prompt reperfusion. Standard echocardiographic modalities might be insufficient to distinguish true aneurysms from pseudo aneurysms, and therefore further studies incorporating a multimodality approach are needed. The higher prevalence in urban teaching hospitals could potentially reflect higher severity, greater use of guidelinedirected imaging and better diagnostic modalities.¹⁴ Lastly, the HCUP-NIS database, does not distinguish incident from prevalent LV aneurysms, so it is conceivable that these may have been present at admission.

In the present study spanning 18 years, LV aneurysms complicated 0.2% to 0.3% of all STEMI and 0.1% to 0.2% of all NSTEMI admissions. In adjusted analyses, there was a slight increase in prevalence during the latter half of the study period. From this administrative database, the exact reason for this uptick could not be defined but is likely be due to increase in routine imaging following myocardial infarction that is consistent with current endorsement by the

Table 2

In-hospital characteristics of AMI admissions with and without LV aneurysm

Characteristic		LV Aneurysm		р
		Yes (N = 17,626)	No (N = 11,604,903)	
AMI type	STEMI	51.0%	37.1%	< 0.001
	NSTEMI	49.0%	62.9%	
STEMI location*	Anterior	31.0%	12.1%	< 0.001
	Inferior	12.3%	16.4%	< 0.001
	Other	7.9%	8.8%	< 0.001
Fibrinolysis		2.0%	2.2%	0.06
Coronary angiography		78.8%	63.6%	< 0.001
Early coronary angiography (day 0)		35.1%	28.0%	< 0.001
Percutaneous coronary intervention		41.5%	34.7%	< 0.001
Coronary artery bypass grafting		21.3%	9.2%	< 0.001
Right heart catheterization		8.9%	3.9%	< 0.001
Pulmonary artery catheterization		2.6%	1.1%	< 0.001
Mechanical circulatory support	Total	12.4%	4.8%	< 0.001
	IABP	11.8%	4.5%	< 0.001
	pLVAD	0.5%	0.2%	< 0.001
	ECMO	0.3%	0.1%	< 0.001
Acute kidney injury		13.2%	11.6%	< 0.001
Invasive mechanical ventilation		8.8%	6.0%	< 0.001
Hemodialysis		0.5%	0.6%	0.21
Ventricular tachycardia/fibrillation		17.6%	8.0%	< 0.001
Mechanical complications	Composite	2.6%	0.2%	< 0.001
	VSD	1.9%	0.1%	< 0.001
	PMR	0.1%	0.0%	< 0.001
	Hemopericardium	0.4%	0.0%	< 0.001
	Cardiac tamponade	0.4%	0.1%	< 0.001
Cardiac arrest		7.1%	5.0%	< 0.001
Pump failure	Composite	26.3%	16.1%	< 0.001
	Cardiogenic shock	10.0%	4.8%	< 0.001
	Systolic heart failure	15.2%	6.9%	< 0.001
	Respiratory failure	10.8%	8.5%	< 0.001
LV thrombus		1.2%	0.1%	< 0.001
Stroke	Composite	3.4%	1.8%	< 0.001
	Ischemic	3.1%	1.6%	< 0.001
	Hemorrhagic	0.4%	0.2%	< 0.001

Represented as percentage. AMI = acute myocardial infarction; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; LV = left ventricular; NSTEMI = non-ST-segment elevation myocardial infarction; pLVAD = percutaneous left ventricular assist device; PMR = papillary muscle rupture; STEMI = ST-segment elevation myocardial infarction; VSD = ventricular septal defect.

* Only in the admissions with a primary diagnosis of STEMI.

Table 3

Clinical outcomes of AMI admissions with and without LV aneurysm

Characteristic		LV Aneurysms		р
		Yes (N = 17,626)	No (N = 11,604,903)	
In-hospital mortality		7.4%	6.2%	< 0.001
Length of stay (days)		7.5 ± 7.3	5.1 ± 5.9	< 0.001
Hospitalization costs (x1000 United States Dollars)		96 ± 135	60 ± 78	< 0.001
Discharge disposition	Home	59.4%	62.5%	< 0.001
	Transfer	7.1%	12.6%	
	Skilled nursing facility	17.1%	13.4%	
	Home with home health care	15.8%	10.6%	
	Against medical advice	0.6%	0.9%	

Represented as percentage or mean \pm standard deviation.

AMI = acute myocardial infarction; LV = left ventricular.

American Heart Association/American College of Cardiology performance and quality measures for adults with AMI.³⁰ The unadjusted temporal trends for in-hospital mortality showed an uptick in the recent years and could be due to older and sicker patients presenting with AMI, however, following adjustment, there were no difference in the inhospital mortality in patients with and without LV aneurysm.

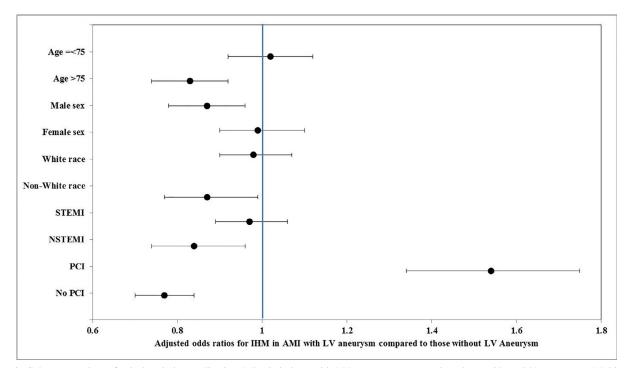


Figure 2. Subgroup analyses for in-hospital mortality in AMI admissions with LV aneurysm compared to those without LV aneurysms. Multivariable adjusted odds ratios (95% confidence intervals)^a for in-hospital mortality in AMI admissions with LV aneurysm compared to those without LV aneurysms. ^aAdjusted for age, sex, race, comorbidity, primary payer, hospital region, hospital location and teaching status, hospital bedsize, type of AMI, cardiogenic shock, cardiac arrest, acute kidney injury, ventricular tachycardia/fibrillation, mechanical complications, pump failure, stroke, left ventricular thrombus, fibrinolysis, coronary angiography, percutaneous coronary intervention, coronary artery bypass grafting, pulmonary artery catheterization, mechanical circulatory support, invasive mechanical ventilation, and acute hemodialysis. Blue line denotes odds ratio of 1.0; odds ratio <1 shows lower in-hospital mortality; LV = left ventricular; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction. (Color version of figure is available online.)

This study has several limitations, despite the HCUP-NIS database's attempts to mitigate potential errors by using internal and external quality control measures. Echocardiographic data, angiographic variables, and hemodynamic parameters were unavailable in this database which limits physiological assessments of disease severity. Importantly, the exact location, extent and hemodynamic consequences of an LV aneurysm that might be noted on echocardiography was not available in this database. Though procedural timing can be timed to day of procedure, that is, a 24-hour interval, we are unable to assess further detailed information such as total ischemic time, doorto-balloon time and risk scoring strategies (for NSTEMI) which might impact the prevalence of LV aneurysms in this study. It is conceivable that the change in ICD coding from ICD-9CM to ICD-10CM may have impacted the temporal trends in this study. Important factors such as the delay in presentation from time of onset of AMI symptoms and treatment-limiting decisions of organ support could not be reliably identified in this database. It is possible that despite best attempts at controlling for confounders by a multivariate analysis, presence of LV aneurysms was a marker of higher morbidity due to residual confounding.

In conclusion, we noted the presence of LV aneurysms in 0.2% of the population. The presence of LV aneurysms was associated with higher morbidity, more frequent complications, higher use of cardiac and noncardiac procedures and greater in-hospital resource utilization, without any differences in in-hospital mortality. Further studies are needed to assess the long-term implications of LV aneurysms in patients suffering an AMI.

Disclosures

All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j. amjcard.2020.07.043.

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